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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,594	07/01/2003	Sheng-Ping L. Hwang	ACAD/0002	3435

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EXAMINER

JOIKE, MICHELE K

ART UNIT	PAPER NUMBER
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1636

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/612,594

Applicant(s)

HWANG ET AL.

Examiner

Michele K. Joike, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 October 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5,20-22 and 46-60 is/are pending in the application.
- 4a) Of the above claim(s) 59 and 60 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5,20-22 and 46-58 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

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DETAILED ACTION

Receipt is acknowledged of a reply to the previous Office Action, filed October 31, 2006. Claims 6-19 and 23-45 are canceled. Claims 46-60 were added. Claims 1 and 20-22 were amended.

Claims 1-5, 20-22 and 46-60 are pending in the instant application. Claims 59 and 60 are drawn to non-elected subject matter and are withdrawn from consideration. Any rejection of record in the previous Office Action, mailed July 31, 2006, that is not addressed in this action has been withdrawn.

Because this Office Action only maintains rejections set forth in the previous Office Action and/or sets forth new rejections that are necessitated by amendment, this Office Action is made FINAL.

Claim Objections

Claims 1, 20, 49 and 58 are objected to because of the following informalities: Claims 1, 20 and 58 contain nonelected sequences. Claim 49 depends from itself. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 and 58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter

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applicant regards as the invention. The claims recite an isolated nucleic acid molecule comprising a zebrafish BMP4 gene and including a nucleic acid sequence of SEQ ID NO: 1. Since SEQ ID NO: 1 is a fragment of BMP4, it is unclear if the isolated nucleic acid molecule includes the sequence of SEQ ID NO: 1, or if the sequence of SEQ ID NO: 1 is separate from the BMP4 gene.

Claim 48 recites the limitation "the recombinant expression vector of claim 46" in line 1. There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 52-57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims an isolated tissue-specific transcriptional regulatory DNA fragment comprising a portion of a zebrafish bone morphogenetic protein 4 gene. The claims read on a broad genus of possible fragments of the isolated DNA molecule.

The written description requirement for a genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other

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physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicants were in possession of the claimed invention. In the instant case, the specification does not sufficiently describe a representative number of fragments that would allow it to still function as a BMP4 protein with tissue-specific transcriptional regulation.

Applicant claims isolated tissue-specific transcriptional regulatory DNA fragments comprising a portion of a zebrafish bone morphogenetic protein 4 gene by function only, without any disclosed or known correlation between the elements and their function. The specification does not teach how to fragment the BMP4 gene in order to maintain the function of the gene. The specification discloses 7 BMP4 fragments in Table 1 that direct tissue-specific expression. For example, 2 DNA constructs, Age1-GFP and Exo III C-GFP, will direct caudal fin expression; 5 expression constructs will not. However, the skilled artisan cannot envision a sufficient number of embodiments of the instant invention from the instant specification because the specification does not disclose which structure or motifs from the gene will retain the ability to direct tissue-specific expression. Nothing is disclosed about the structures of Age1-GFP or Exo III C-GFP that would identify the properties of those fragments that allow for directed expression.

The state of the art at the time of filing does not provide sufficient information on the subject to overcome the deficiencies of the instant specification. There is no description in the art that allows one to envision a representative number of derivatives by disclosing structural or functional features of the possible derivatives so that one of

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skill in the art could envision the claimed invention. Thus the skilled artisan cannot consult the art at the time of filing to envision a sufficient number of embodiments of the instant invention to see that the applicant was in possession of the claimed genus.

Neither the specification of the instant application or the state of the art at the time of filing teaches a structure-function relationship for a representative number of fragments. As a result, the skilled artisan would not be able to envision the claimed invention. Therefore applicant has not satisfied the written description requirement to show the skilled artisan that they were in possession of the claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5, 20-22, 46-48, 50-51 and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Hwang et al.

Applicants teach an isolated DNA molecule comprising a zebrafish BMP4 gene and including a nucleotide sequence of SEQ ID NO: 1, an expression vector comprising a portion of the DNA molecule and the cell containing the isolated DNA molecule. They also teach an isolated tissue-specific transcriptional regulatory DNA fragment comprising a DNA sequence of zebrafish bone morphogenetic protein 4 gene which includes SEQ. ID NO. 1, as well as an isolated DNA molecule comprising a zebrafish

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bone morphogenetic protein 4 gene, a recombinant expression vector comprising a portion of the isolated DNA molecule, wherein the portion of the isolated DNA molecule is operatively linked to a nucleotide sequence encoding a heterologous expression product. They also teach a cell comprising the isolated DNA molecule and an isolated tissue-specific transcriptional regulatory DNA fragment comprising a portion of the isolated DNA molecule.

Hwang et al (DNA and Cell Biol. 16(8): 1003-1011, 1997, specifically pp. 1003, 1005, 1006 and Figure 2 (reference B18 on the IDS)) teach the nucleotide sequence of the zebrafish BMP4 gene. Applicants teach an isolated DNA molecule comprising a zebrafish BMP4 gene and including a nucleotide sequence of SEQ ID NO: 1, which is being interpreted as the zebrafish BMP4 gene including two nucleotides of SEQ ID NO: 1, since a nucleotide sequence can mean just two or more nucleotides. In figure 2 of Hwang et al, the coding sequence of the zebrafish BMP4 gene including two nucleotides, TT, from SEQ ID NO: 1 are disclosed. The reference also teaches a 270 bp fragment (portion) generated from PCR and introduced into the vector, pQE30. The fragment is linked to a heterologous gene to produce a fusion protein. pQE30 was transformed into *E. coli* cells. Zebrafish BMP4 is a tissue-specific transcriptional regulatory which directs expression of in the heart, caudal fin, digestive tract and testes. They also teach BMP4 harvested from zebrafish embryos.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 4 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hwang et al in view of Chin et al and in further view of Bayer et al.

Applicants teach an isolated DNA molecule comprising a zebrafish BMP4 gene and including a nucleotide sequence of SEQ ID NO: 1, an expression vector comprising a portion of the DNA molecule, and that the portion of the isolated DNA molecule is operatively linked to a nucleotide sequence encoding a heterologous expression product, wherein the heterologous expression product is a reporter protein, specifically β -galactosidase.

Hwang et al teach all of the limitations as described above, however, they do not teach the use of a reporter protein.

Chin et al (Dev Genes Evol 207:107-114, 1997, specifically p. 108 (reference B6 on the IDS)) teach the zebrafish BMP4 gene, wherein a 1600 bp fragment was inserted into the vector, pCRII, which contains a *lacZ* gene. The *lacZ* gene encodes the heterologous reporter protein, β -galactosidase.

Bayer et al (Development 115: 421-426, 1992, specifically pp. 421 and 425) teach a zebrafish expressing the *lacZ* gene.

The ordinary skilled artisan, desiring to use the *lacZ* gene as the reporter protein in an expression vector with the BMP4 gene, would have been motivated to combine the teachings of Hwang et al on an isolated DNA molecule comprising a zebrafish BMP4 gene and including a nucleotide sequence of SEQ ID NO: 1, an expression vector comprising a portion of the DNA molecule, and that the portion of the isolated DNA molecule is operatively linked to a nucleotide sequence encoding a heterologous expression product, with the teachings of Chin et al, teaching zebrafish BMP4 gene, wherein a 1600 bp fragment was inserted into the vector, pCRII, which contains a *lacZ* gene, with Bayer et al teaching a zebrafish expressing the *lacZ* gene, because Bayer et al state that *lacZ* expression may serve as a valuable morphological marker to study patterns of gene expression at the cellular level. It would have been obvious to one of ordinary skill in the art to use *lacZ* linked to the BMP4 gene because a *lacZ* fusion can integrate functionally into the zebrafish genome. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it

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must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Allowable Subject Matter

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele K. Joike, Ph.D. whose telephone number is 571-272-5915. The examiner can normally be reached on M-F, 9:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone

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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michele K Joike, Ph.D.
Examiner
Art Unit 1636


DAVID GUZO
PRIMARY EXAMINER